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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/316,048	05/21/99	DESGROSEILLERS L	10875.77

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EXAMINER	
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ART UNIT	PAPER NUMBER
1632	16

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No.	Applicant(s)	
	09/316,048	DESGROSEILLERS ET AL.	
	Examiner	Art Unit	
	Ram R. Shukla	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *21 December 2000 and 05 March 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-23* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 9-18* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4-8 and 19-23* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)
16) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
17) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4* .
18) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
19) ☐ Notice of Informal Patent Application (PTO-152)
20) ☐ Other:

DETAILED ACTION

1. Amendment filed 12-21-00 has been entered.

2. Applicant's election of the invention of group II, claims 4-8 in Paper No. 11 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

3. Claims 1-3 and 9-18 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No. 11.

4. Supplementary amendment filed 3-5-01 has been entered.

5. Amendment to claim 4 has been entered.

6. New claims 19-23 have been entered.

7. Claims 4-8 and 19-23 are instantly under consideration.

8. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Canada on 5-22-1998. It is noted, however, that applicant has not filed a certified copy of the application (#2,238,656) as required by 35 U.S.C. 119(b) and therefore priority is not granted.

9. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 C.F.R. § 1.821(a)(1) and (a)(2) (see figure 1, page 43 lines 6 and 7, page 45, lines 13, 14, 23, and 24). However, this application fails to comply with the requirements of 37 C.F.R. §§ 1.821 (d) which states "Where the description or claims of a patent application discuss a sequence that is set forth in the "Sequence Listing " in accordance with paragraph (c) of this section, reference must be made to the sequence by use of the sequence identifier, preceded by "SEQ ID NO: " in the text of the description or claims,

even if the sequence is also embedded in the text of the description or claims of the patent application."

Appropriate correction is required.

10. The specification is objected to because it is not a permanent copy as required by 37 CFR 1.52(a). Reference is made to all of the specification including figures.

It is noted that the specification (disclosure, claims, figures, etc.) has been submitted on thermal fax paper. Some parts of the specification have faded and are hard to read.

Applicant is required to submit permanent copy of the entire specification, including figures. See MPEP § 608.01.

Claim Rejections - 35 USC § 101

11. Claims 4-8 and 19-23 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility.

Applicant is referred to utility guidelines published in Federal Register January 5, 2001, Volume 66, Number 5, Pages 1092-1099.

When determining whether an applicant has described the utility of invention, one has to determine whether the applicant has described a well-established utility. If not, has the application made any assertion of specific, substantial and credible utility. A credible utility is assessed from the standpoint of whether a person of ordinary skill in the art would accept that the recited or disclosed invention is currently available for use. In contrast to general utility, a specific utility will be specific to the claimed subject matter. A substantial utility defines a real world utility of the invention and utilities that require or constitute carrying our further research to identify or reasonably confirm a "real world" context use are not

substantial utility (see utility guidelines, in Federal Register January 5, 2001, Volume 66, Number 5, Pages 1092-1099).

In case of an isolated DNA, when the major utility of the DNA is as a probe, it is asked if the DNA is specific to a particular organism or is it discriminatory towards a certain organism. For example, if said DNA was used as probe, one can identify an organism with certainity. In other words, it will specifically hybridize to the genome of a certain organism. In case of DNA encoding protein claims, one asks whether the protein has an established and specific function.

In the instant case, the invention of claim4 is drawn to a nucleic acid comprising a polynucleotide that has at least 95% sequence identity to 1-577, 2-377, 82-577, 83-577, 1-487, 2-487, SEQ ID NO 27, or polynucleotides complementary to all the above that encode a staufen polypeptide. Claim 19 recites a nucleic acid molecule that comprises a polynucleotide that is at least 95% identical to sequence of SEQ ID NO 1, 3, 5, 7, 9, a nucleotide complementary to all these, and a nucleotide sequence that hybridizes to all these polynucleotides. Claims 5-8 and 20-23 are drawn to vectors comprising the nucleic acids of claim 4 and 19 and host cells comprising these vectors.

It is noted that the specification does not clearly assert what is the utility of the claimed invention. Page 4, line 20 continued through line 8 of page 7 of the specification lists problems related to mRNA transport in mammals, understanding the mechanism of the structure-function relationship of mammalian staufen, need to provide means to target molecules to RNA viruses, need to find assay for identifying and isolating molecules that modulate the interaction between the RNA genome incorporation into RNA virions etc. Likewise, on page 69, the specification notes "In light of the negative impact of hStau overexpression on viral infectivity, hStau may be a suitable target for an anti-HIV-1 strategy. Furthermore, in light of the demonstration that hStau is incorporated into other retroviruses as well as Reovirus, staufen may be a suitable target for anti-RNA-virus therapy in general" (see lines 12-16 on page 69). All these statements using the phrase "may be" indicate that the claimed invention does not have a specific and substantial utility and the only utility which can be thought about would be for further research which

is not a real world utility. An apparent or implied utility of the claimed polynucleotides could be to make a protein. However, these utilities are not specific because the specification does not teach what is the biological activity of the staufen protein. While the specification discloses characterization of the sequence of the protein, nucleic acid sequence encoding the protein, comparison of the protein structure with that in Drosophila and localization in the subcellular compartments (see examples 4-15), the specification fails to teach what is the function of the protein. In fact, the specification on page 55, lines 6-8, notes "Although its precise role is still unclear, its biochemical and molecular properties strongly suggest that it is involved in mRNA transport and/or localization." This statement clearly indicates that further research is required to understand the role of staufen. Therefore, in the absence of a clearly defined activity, the only utility for the claimed polynucleotides would be a research to further characterize the protein. While the specification teaches that the polynucleotide of the instant invention is a homologue of Drosophila staufen, there are clear and considerable differences between the two, for example, mammalian staufen does not contain the first dsRNA binding domain and the long N-terminal sequence that binds to oskar protein (see lines 25-27 on page 49). If so, it is not clear whether one can assume that the function/role of mammalian staufen is the same as of the Drosophila. Again, in the absence of a clear teaching from the specification, an asserted specific and substantial utility of the claimed polynucleotides is not clear.

While another implied or apparent utility could be to use the claimed nucleotides as a probe, there is only 53% sequence similarity between the nucleic acid encoding human staufen and Drosophila staufen. Sequence comparison of the two sequences (at the most) showed sequence similarity in a region of only 10 amino acids (see sequence comparison results with Accession NO M69111, Databse GenEmbl, 4-26-1993), which indicates that the two sequences are very divergent. Therefore, based on the sequence similarity data the use of probe for identifying homologous sequences could not be considered a specific and substantial utility because if the activity of SEQ ID NO 6 is not well established, what would be the

utility of another sequence that hybridizes to this sequence, again it would be to further characterize the claimed invention.

In view of the foregoing, one skilled in the art would not be able to readily attribute a well established biological function/role to the protein encoded by the instantly claimed nucleic acid due to the absence of an evidence of significant sequence similarity. In view of such, it is unclear as to what activity could be attributed to the deduced amino acid sequence of the claimed nucleic acid. Due to such a low sequence similarity, a nucleic acid probe would not be able to differentiate between the claimed sequence from human source and another polynucleotide from another organism. While the specification does not assert any specific utility for the claimed invention, even apparent and implied utilities could not be considered specific and/or substantial utility, since no function can be ascribed to the gene. Applicants are advised to clearly point out the sections of the specification which disclose specific and substantial utility of the claimed invention.

12. Claims 4-8 and 19-23 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

13. Claims 4-8 and 19-23 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

While determining whether a specification is enabling, one considers whether the claimed invention provides sufficient guidance to make and use the claimed invention, if not, whether an artisan would have required undue experimentation to make and use the claimed invention and whether working examples have been provided. When determining whether a specification meets the enablement requirements, some of the factors that need to be analyzed are: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of

ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and whether the quantity of any necessary experimentation to make or use the invention based on the content of the disclosure is "undue".

Furthermore, USPTO does not have laboratory facilities to test if an invention will function as claimed when working examples are not disclosed in the specification, therefore, enablement issues are raised and discussed based on the state of knowledge pertinent to an art at the time of the invention, therefore skepticism raised in the enablement rejections are those raised in the art by artisans of expertise.

In the instant case, the claimed invention drawn to a nucleic acid comprising a polynucleotide that has at least 95% sequence identity to 1-577, 2-377, 82-577, 83-577, 1-487, 2-487, SEQ ID NO 27, or polynucleotides complementary to all the above that encode a staufen polypeptide. The claimed invention is also drawn to a nucleic acid that comprises polynucleotide that is at least 95% identical to sequence of SEQ ID NO 1, 3, 5, 7, 9, a nucleotide complementary to all these, and a nucleotide sequence that hybridizes to all these polynucleotides. Claims are also drawn to vectors comprising the claimed nucleic acids and host cells comprising the vectors. The specification is not enabling for the claimed invention because the specification does not provide sufficient guidance and working example as to how an artisan of skill would have made and used the claimed invention and the artisan would have required undue experimentation to make and use the claimed invention as discussed below.

While the specification teaches the method for cloning of human staufen encoding cDNA, antibody for staufen protein, binding of staufen protein to RNA, tubulin binding assay, generation of splicing variants of the human staufen protein etc (examples 1-9). While example 10 discloses that both human and mouse staufen bind to dsRNA, there is no nucleotide sequence specificity (see lines 23-25 on page 50) of the binding. The specification does not provide any clear guidance as to what is the function/biological activity of the human staufen protein. While the specification teaches that the polynucleotide of the instant invention is a homologue

of Drosophila staufen, there are clear and considerable differences in the sequence structure of the two proteins, for example, mammalian staufen does not contain the first dsRNA binding domain and the long N-terminal sequence that binds to oskar protein (see lines 25-27 on page 49). Additionally, the specification discloses that the human staufen contains a tubulin binding domain which is not present in Drosophila (see lines 1-3 on page 50). If so it is not clear whether one can safely assume that the function/role of mammalian staufen is the same as the Drosophila and therefore an artisan would not know how to use the claimed polynucleotides.

Additionally, the specification on page 55, lines 6-8, notes "Although its precise role is still unclear, its biochemical and molecular properties strongly suggest that it is involved in mRNA transport and/or localization." This statement clearly indicates that the function of the protein encoded by the claimed polynucleotides is not known and defined and therefore, further research would be required to understand the role of staufen. Since the specification does not provide sufficient guidance as to how an artisan of skill have used the claimed polynucleotides and for what purpose, an artisan would have to carry out extensive experimentation and research to figure our the function of the protein encoded by the claimed invention which would have been undue.

It is further noted that the specification fails to clearly teach how to use the claimed polynucleotides. For example, on page 69, the specification notes "In light of the negative impact of hStau overexpression on viral infectivity, hStau may be a suitable target for an anti-HIV-1 strategy. Furthermore, in light of the demonstration that hStau is incorporated into other retroviruses as well as Reovirus, staufen may be a suitable target for anti-RNA-virus therapy in general" (see lines 12-16 on page 69). However, the specification fails to teach how to use the claimed invention for all these purposes. It is noted that all these statements in the specification using the phrase "may be" indicate further research would be required for using the claimed polynucleotides.

Next, claims 4 and 19 recite fragments of the claimed nucleotides such as those encoding 83-577 or 1-497 or 2-487, however, it is not clear how would an artisan have known how to use the claimed fragments, particularly when the

activity of the full length protein was not known and established. Furthermore, regarding the sequences of SEQ ID NO 1, 3, 7, and 9, it is noted that the specification fails to teach how to use these nucleotide sequences because the specification does not discuss the function of these polynucleotides. Based on the sequence disclosure, in a particular SEQ ID NO, while an artisan may be able to know the sequence structure, an artisan would not know how to use these nucleic acids and for what. Regarding the nucleic acids that are 95% identical to the claimed sequences, it is noted that if an artisan did not know how to use the wild type sequence, how would one know how to use sequences that have alterations in the sequences. For example, which 5% sequences of the claimed nucleic acids to alter and whether such alterations would be distributed along the full length of the sequence or concentrated in certain regions. If one had to use sequence that was 95% identical to SEQ ID NO 5, one could change upto about 175 nucleotides since SEQ ID NO 5 consists of 3506 nt and an artisan would not know which 175 nucleotides to change that the resultant encoded protein is still functional. Alternatively, if one had to change only encoding sequences, one could change upto 85 nucleotides which would translate into 28 amino acids. Again the specification does not teach which 85 nucleotides could be changed without altering the activity of the encoded protein. It is recognized in the prior art that the function of a protein depends on the sequence of its amino acids in a certain pattern, conformation of the protein due to the amino acid sequence, and the functional properties of the different parts of the protein (see second paragraph in Rudinger J in Peptide Hormones. Editor Parsons JA. Pages 1-7, 1976, University Park Press, Baltimore). Rudinger further add, "The significance of particular amino acids and sequences for different aspects of biological activity can not be predicted *a priori* but must be determined from case to case by painstaking experimental study" (see conclusion on page 6). Similar arguments are valid regarding each of the claimed sequences.

If one had to use the claimed nucleotides as a probe, it is not clear whether a probe based on the claimed invention would have resulted in finding a nucleic acid that would encode a protein that would have the function of the protein encoded by

the claimed invention. It is noted that the sequences of the claimed invention were isolated based on sequence similarity with the Drosophila sequence (see example 1), however, as discussed above there are considerable differences between the human and Drosophila staufen sequences and the specification does not teach whether they both bind to the same RNA or perform same function. Therefore based on the sequence similarity data the use of probe for identifying homologous sequences would yield a nucleic acid which would encode a protein with same function. Again, an artisan would have go through extensive experimentation to characterize the claimed polynucleotides and such would have been undue.

Therefore, in view of the breadth of the claims and the lack of guidance provided by the specification as well as the unpredictability of the art, one of ordinary skill in the art at the time of the invention would have required an undue amount of experimentation to make and use claimed polynucleotides, host cells, vectors, and transgenic insects.

14. Claim 4 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

It is noted that applicants have added SEQ ID NO 27 in the sequence listing. Applicants in their supplementary amendment have contended that SEQ ID NO 27 is a C.elegans sequence which was present in figure 1'. However, figure 1 is an alignment of sequences from Drosophila, human and C.elegans which has huge gaps in the sequences as illustrated in figure 1. It is not clear whether the sequence in SEQ ID NO 27 is the same as the sequence disclosed in figure 1' and there is no way of knowing it since SEQ ID NO 27 has not been filed as a SEQ ID before. Accordingly, SEQ ID NO 27 is considered a new matter.

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claim 4-8 and 19-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 4 and 23 are indefinite because they are drawn to "an isolated nucleic molecule" and the specification does not define what is meant by "an isolated nucleic molecule". For examination purposes, the term is interpreted as "an isolated nucleic acid molecule."

Claim 4 (b) is indefinite because it is missing "to" between "83" and "about" in line 2.

Claim 4 is also indefinite because it recites the term "about." Since "about" is a relative term, the metes and bounds of the claimed subject matter is not clear. For example, about 82 to about 577 could be interpreted as 1-577 or 10-50 or anything. Clarification is required.

Claims 5 and 20 recite the limitation "said isolated nucleic acid molecule" in line 1. There is insufficient antecedent basis for this limitation in the claims because the parent claims do not recite the term.

Claim 19 is indefinite because it recites the term "high stringency condition." It is noted that "high stringency condition" is relative and what would considered high stringent in once situation may not be stringent enough in another codition.

Claim Rejections - 35 USC § 102

17. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless -
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

18. Claim 19 is rejected under 35 U.S.C. 102(b) as being anticipated by Marra et al (Accession No. AA122533, Database EST, 2-17-97).

Marra et al teach a 522 bp nucleic acid sequence that has 99.8% best local sequence similarity with nt 2248-2770 of SEQ ID NO 9 and therefore would hybridize to SEQ ID NO 9 under stringent conditions.

Accordingly the invention of claim 19 (g) is anticipated by Marra et al.

19. Claim 19 is rejected under 35 U.S.C. 102(a) as being anticipated by Banfi et al (Accession No. G30939, Database GenEmbl, 9-29-98; Nature Genetics 13:167-174, 1996).

Banfi et al teach a 385 bp nucleic acid sequence that has 99.2% sequence similarity with nt 2705-3089 of SEQ ID 1, 3069-3453 of SEQ ID NO 5, and 2911-3295 of SEQ ID NO 7 and therefore would hybridize to SEQ ID NO 1, 5, and 7 under stringent conditions.

Accordingly the invention of claim 19 (g) is anticipated by Banfi et al.

20. No claim is allowed.

21. The nucleic acid sequences of SEQ ID NO 1, 3, 5, 7, and 9 are free of the prior art of record.

Applicants are advised to submit a clean version of each amended claim (without underlining and bracketing) according to § 1.121(c) and a copy of all the pending/under consideration claims. For instructions, Applicants are referred to http://www.uspto.gov/web/offices/dcom/olia/aipa/index.htm.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ram R. Shukla whose telephone number is (703) 305-1677. The examiner can normally be reached on Monday through Friday

from 7:30 am to 4:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached on (703) 305-6608. The fax phone number for this Group is (703) 308-4242. Any inquiry of a general nature, formal matters or relating to the status of this application or proceeding should be directed to the Kay Pinkney whose telephone number is (703) 305-3553.

Ram R. Shukla, Ph.D.

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